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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,169	GRUSBY ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,13 and 17-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 13, 17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment

1a. Receipt of Applicants' amendment and arguments, filed on 13 July 2006 is acknowledged.

Status of Claims:

1b. Claims 1-10, 12, 14-16 have been cancelled. Thus, claims 11, 13, 17-25 are pending and under consideration.

1c. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The following previous objections and rejections are withdrawn in light of Applicants' amendment filed 07/13/06.

(I) All of the rejections made against cancelled claims 12 and 14-16 are moot.

(II) The rejection of claims of 11, 13, 24 and 25 made under 35 U.S.C. 112, second paragraph, is withdrawn, because the claims now recite the article "the" when referring to IL-21R.

Information Disclosure Statement:

3a. "Amino Acid Sequence Comparisons" cited on the PTO-1449 form submitted by Applicants on 07 June 2006 have been placed in the case, but have not been considered, because they do not comply with 37 CFR 1.98(a)(2) requirements, since they fail to identify each publication by author and accession number. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the

requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 C(1).

Response to Applicants' arguments:

Claim Rejections under 35 U.S.C. §112:

4a. Claims 11, 13, 20-25 stand rejected rejected under 35 U.S.C. 112, first paragraph for not satisfying the written description requirements as set forth in the previous office actions.

Applicants submit that the instant claims encompass a soluble receptor that displays solubility, that is capable of antagonizing IL-21R activity, that comprises an extracellular domain of an IL-21R, which contains an extracellular domain that is capable of binding IL-21 or fragment thereof and contains an extracellular domain that is least 85% identical to amino acids 20 to 235 of human IL-21R (SEQ ID NO:4) and is capable of inhibiting or reducing the differentiation of a Th cell precursor population into Th2 or increasing IFN-γ levels in a T cell. Applicants point to the existence of a murine IL-21R that shares 62% homology to the polypeptide of SEQ ID NO:4. Thus Applicants argue that the claims encompass a soluble receptor that varies at most 15% from a known sequence, and since they describe IL-21R sequences that can differ by about 38%, Applicants were in possession of the claimed genius. Applicants also argue that the specification discusses IL-21R sequences with varying degrees of identity to the disclosed human IL-21R, thus the soluble receptor may vary from the human IL-21R sequence, as long as it retains the ability to bind an IL-21 ligand. Applicants contend that one skilled in the art could align the human IL-21R and mouse IL-21R sequences

disclosed in the specification to identify regions and residues of IL-21R that are conserved or variable and thus identify those residues amenable to substitutions. Applicants further argue that one of ordinary skill in the art would recognize that Applicants were in possession of a genius of soluble IL-21R as recited in the claims. Applicants argue that the specification "need not teach, and preferably omits, what is well known in the art". Applicants submit that alignment of a family of common gamma chain receptors derived from different species would indicate regions of IL-21R that should not be significantly altered or regions that should be altered only with similar amino acids. Applicants submit several references that teach receptors that share some identity with IL-21R and argue that one skilled in the art would follow these teachings and figure out which residues of IL-21R could be modified and which ones should be conserved.

These arguments have been considered but are not deemed persuasive. Firstly, Applicants have not disclosed a soluble IL-21R that comprises an extracellular domain of IL-21R that is at least 85% identity to the extracellular portion of the 1L-21R that binds IL-21 or to IL-21 fragment, which is capable of antagonizing IL-21R activity, reduces or inhibits the differentiation of Th precursor cell population into a Th2 and is capable of increasing IFNγ. The specification describes the structure of the full length of the human IL-21R (SEQ ID NO:4) and teaches that the extracelullar region comprises amino acids 20-235 of SEQ ID NO:4, (see page 4, lines 12-18 and page 5, lines 1-12). The specification also shows that IL-21 inhibits IFN-gamma levels and potentates Th2 responses, (see examples 2 and 3). Therefore, an antibody against IL-

21R or a soluble IL-21R would be expected to bind to IL-21 and antagonize IL-21R activity. However, while the specification contemplates a soluble IL-21R that is at least 85% identical to amino acids 20 to 235 of SEQ ID NO: 4, that is capable of binding IL-21 receptor and displays all of the recited activities, it fails to disclose one single variant that possess the recited activities. Therefore, Applicants were not in possession of any variant that exhibits the desired activities. The specification does not describe which amino acids of amino acids 20 to 235 of SEQ ID NO: 4, can be altered without altering the desired activities. The instant specification does not demonstrate that the murine IL-21R which shares 62% homology to the polypeptide of SEQ ID NO:4, retains the functional requirements recited in claims 11 and 13. The issue is not the existence of receptors that share 85% homology to residues 20-235 of SEQ ID NO:4, but whether said receptors also retain the desired activity. It is acknowledged that a patent need not teach, and preferably omits what is well known in the art, however, the specification must teach the novel aspects of the invention. See Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997):

"[T]hat the omission of minor details does not cause a specification to fail to meet the enablement requirement. .... It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". The Genentech court also held that [w]hile every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention". Id. In this case, as in Genentech, the specification does not provide the "reasonable detail .....to enable members of the public to understand and carry out the invention".

In the instant case, although the specification contemplates IL-21R sequences with varying degrees of identity to the disclosed human IL-21R, it does not disclose one

single variant that retains the desired activity. The issue is not whether the skilled artisan can figure out which amino acids residues to modify and which to conserve, but whether the specification discloses variants that retain the recited functions, to indicate that Applicants were in possession of the claimed genius. In the instant case, there is not even one single variant that retains the recited activity. Accordingly, the instant specification only describes the full length IL-21R that possess the recited activities, and teaches an extracellular domain which comprises amino acids 20- 235 of SEQ ID NO:4, but fails to describe an extracellular domain which comprises an amino acid sequence that is at least 85% identical to amino acids 20- 235 of SEQ ID NO:4 that possess the recited activities.

Claim Rejections Under 35 U.S.C. § 112, first paragraph: Enablement:

4b. Claims 11, 13, 20-25 stand rejected under 35 U.S.C. 112, first paragraph for not enabling the full scope of the claimed invention, as set forth in the office action mailed on 07 March 2006.

Applicants argue that the claimed methods specifically recite that only IL-21 or IL-21R antagonists are to be employed in the pending method claims and therefore, although certain soluble IL-21Rs may act as agonists, agonist soluble receptors are not within the scope of the presently claimed methods. Applicants submit that IL-21R antagonists (in the form of a soluble fusion protein containing an extracellular domain of an IL-21R fused to an Fc fragment) have also been used to treat the symptoms of systemic lupus erythematosus (SLE) in an MRL-Fast pr mouse model of lupus, thus the specification enables the therapeutic use of IL-21R.

This argument is deemed persuasive in part. It is acknowledged that the claimed method encompasses the use of a soluble IL-21R as an antagonist and therefore, soluble receptors that may act as agonists are irrelevant. Furthermore, the therapeutic usefulness of IL-21R antagonist is acknowledged. However, while the specification discloses a full length soluble IL-21R that possess the recited activities, it is non-enabling for a soluble IL-21R that comprises an extracellular domain of IL-21R that is at least 85% identity to the extracellular portion of the 1L-21R that posses the recited activities. Furthermore, it is known for proteins that even a single amino acid change or mutation can destroy the function of protein in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over proteins of related function upon a significant amount of further research (see Wells, 1990, Biochemistry 29:8509-8517).

To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of which 15% of SEQ ID NO:4, to alter and produce a receptor that still retains the desired activity. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation.

Claim rejections-35 USC § 103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 13, 17-23, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasaian et al (April 2002) in view of Brenne et al May 2002).

Claims 13, 17-23 and 25 are drawn to a method for increasing interferon gamma levels in a T cell with an antagonist of IL-21, wherein said antagonist is anti-IL-21R antibody or soluble IL-21R.

Kasaian et al teach that IL-21 enhances interferon gamma production in T cells, (see abstract, pages 561-562, page 567 column 1 and figure 5).

Brenne et al disclose a method of using anti-IL-21R antibodies or soluble IL-21R to completely neutralize IL-21 activities, (see page 3757, column 1, and page 3760 top of column 1). However, Brenne et al do not disclose a method of increasing interferon

gamma by in a T cell population with an antagonist of IL-21, wherein said antagonist is anti-IL-21R antibody or soluble IL-21R.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to develop a method OF increasing interferon gamma in a T cell population with an antagonist of IL-21, wherein said antagonist is anti-IL-21R antibody or soluble IL-21R, by combining the teachings of Brenne et an and Kasaian et al, because Brenne et al teach that anti-IL-21R antibodies and soluble IL-21R are both capable of completely neutralizing IL-21 activity, while Kasaian et al teach that IL-21 leads to inhibition of interferon gamma in a T population.

One of ordinary skill in the art would have been motivated to increase interferon-gamma, because IFN-γ has antiviral, immunoregulatory, and anti-tumour properties and is useful in treating infections.

Conclusion:

7. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
25 September 2006

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER